CLAIMS

1. A method for treating $CD40^+$ malignancies comprising administering a therapeutically effective amount of an antibody or antibody fragment which binds to CD40L thereby inhibiting CD40/CD40L interaction or CD40 signaling.

2. The method of Claim 1, wherein the $CD40^+$ malignancy is a B-cell lymphoma or a B-cell leukemia.

3. The method of Claim 2, wherein the B-cell lymphoma is Hodgkin's Disease (HD) or Non-Hodgkin's Lymphoma (NHL).

4. The method of Claim 3, wherein the NHL is low grade, intermediate grade or high grade.

5. The method of Claim 3, wherein the NHL is selected from the subtype group consisting of: small lymphocytic, follicular and predominantly small cleaved cell, follicular and mixed small cleaved and large cell type, follicular and predominantly large cell type, diffuse small cleaved cell, diffuse mixed small and large cell, diffuse large cell, large cell immunoblastic, lymphoblastic, small non-cleaved Burkitt's and non-Burkitt's type, AIDS-related lymphomas, angioimmunoblastic lymphadenopathy, mantle cell lymphoma, and monocytoid B-cell lymphoma.

6. The method of Claim 2, wherein the B-cell leukemia is a chronic B-cell leukemia, acute lymphoblastic leukemia of a B-cell lineage, or chronic lymphocytic leukemia of a B-cell lineage.

7. The method of Claim 2, wherein the antibody or antibody fragment which binds to CD40L is IDEC-131, 3E4, 2H5, 2H8, 4D9-8, 4D9-9, 24-31, 24-43, 89-76 or 89-79.

8. The method of Claim 7, wherein the antibody or antibody fragment is chimeric, bispecific, human or humanized.

9. The method of Claim 2, wherein the antibody fragment is Fab, Fab', scFv or $F(ab')_2$.

10. The method of Claim 2, further comprising administering a therapeutically effective amount of a second antibody or fragment thereof, a chemotherapeutic, a combination of chemotherapeutic agents and/or a radiotherapy.

11. The method of Claim 10, wherein the radiotherapy is external radiation treatment or a radiolabeled antibody.

12. The method of Claim 11, wherein the radiolabeled antibody is radiolabeled IDEC-131, RITUXAN®, or B1 or fragments thereof.

13. The method of Claim 12, wherein the radiolabeled antibody is radiolabeled with ^{123}I, ^{125}I, ^{131}I, ^{111}In, ^{131}In ^{32}P, ^{64}Cu, ^{67}Cu, ^{211}At, ^{177}Lu, ^{90}Y, ^{186}Re, ^{212}Pb, ^{212}Bi, ^{47}Sc, ^{105}Rh, ^{109}Pd, ^{153}Sm, ^{188}Re, ^{199}Au, ^{211}At, and ^{213}Bi.

14. The method of Claim 10, wherein the chemotherapeutic agent for treating HD is any one or more of the following: an alkylating agent, a vinca alkaloid, procarbazine, methotrexate or prednisone.

15. The method of Claim 10, wherein the chemotherapeutic agent for treating NHL is any one or more of the following: an alkylating agent, cyclophosphamide, chlorambucil, 2-CDA, 2'-deoxycoformycin, fludarabine, cytosine arabinoside, cisplatin, etoposide or ifosfamide.

16. The method of Claim 10, wherein the combination of chemotherapeutic agents for treating HD is: MOPP, ABVD, ChlVPP, CABS, MOPP plus ABVD, MOPP plus ABV, BCVPP, VABCD, ABDIC, CBVD, PCVP, CEP, EVA, MOPLACE, MIME, MINE, CEM, MTX-CHOP, EVAP or EPOCH.

17. The method of Claim 10, wherein the combination of chemotherapeutic agents for treating NHL is: CVP, CHOP, C-MOPP, CAP-BOP, m-

BACOD, ProMACE-MOPP, ProMACE-CytaBOM, MACOP-B, IMVP-16, MIME, DHAP, ESHAP, CEPP(B) or CAMP.

18. The method of Claim 10, wherein the chemotherapeutic agent for treating a B-cell leukemia is at least one of the following: anthracycline, cyclophosphamide, L-asparginase and a purine analog.

19. The method of Claim 10, wherein the combination of chemotherapeutic agents for treating a B-cell leukemia is: vincristine, prednisone, anthracycline and cyclophosphamide or asparginase; vincristine, prednisone, anthracycline, cyclophosphamide and asparginase; CHOP; CMP; CVP; COP or CAP.

20. The method of Claim 10, wherein the second antibody is selected from the group consisting of an anti-CD20 antibody, anti-CD19 antibody, anti-CD22 antibody, and anti-CD40 antibody.

21. The method of Claim 21, wherein the anti-CD20 antibody is RITUXAN® or a fragment thereof or B1 or a fragment thereof.

22. A method of treating a $CD40^+$ malignancy comprising the step of administering an anti-CD40L antibody or fragment thereof wherein the anti-CD40L antibody or antibody fragment blocks CD40-CD40L interaction or inhibits CD40 signaling; and administering a second antibody or fragment selected from the group consisting of an anti-CD20, anti-CD40, anti-CD19, and anti-CD22 antibody or fragment thereof.

23. The method of Claim 22, wherein the $CD40^+$ malignancy is a B-cell lymphoma or a B-cell leukemia.

24. A combination therapy for the treatment of a $CD40^+$ malignancy comprising a CD40L antagonist and at least one of the following (a) a chemotherapeutic agent or a combination of chemotherapeutic agents, (b) a radiotherapy, (c) an anti-CD20 antibody or fragment thereof and (d) anti-CD40

antibody or fragment thereof, (e) an anti-CD19 antibody or fragment thereof, and (f) an anti-CD22 antibody or fragment thereof.

25. The method of Claim 24, wherein the radiotherapy is external radiation treatment or a radiolabeled antibody.

26. The method of Claim 25, wherein the radiolabeled antibody is radiolabeled with ^{123}I, ^{125}I, ^{131}I, ^{111}In, ^{131}In ^{32}P, ^{64}Cu, ^{67}Cu, ^{211}At, ^{177}Lu, ^{90}Y, ^{186}Re, ^{212}Pb, ^{212}Bi, ^{47}Sc, ^{105}Rh, ^{109}Pd, ^{153}Sm, ^{188}Re, ^{199}Au, ^{211}At, and ^{213}Bi.

27. The combination therapy of Claim 24 wherein the $CD40^{+}$ malignancy is a B-cell leukemia or B-cell lymphoma.

28. The combination therapy of Claim 27, wherein the B-cell lymphoma is HD or NHL.

29. The combination therapy of Claim 28, wherein the NHL is low grade, intermediate grade or high grade.

30. The combination therapy of Claim 28, wherein the NHL is selected from the subtype group consisting of the following: small lymphocytic, follicular and predominantly small cleaved cell, follicular and mixed small cleaved and large cell type, follicular and predominantly large cell type, diffuse small cleaved cell, diffuse mixed small and large cell, diffuse large cell, large cell immunoblastic, lymphoblastic, small non-cleaved Burkitt's and non-Burkitt's type, AIDS-related lymphomas, angioimmunoblastic lymphadenopathy, mantle cell lymphoma and monocytoid B-cell lymphoma.

31. The combination therapy of Claim 28, wherein the B-cell leukemia is a chronic B-cell leukemia, acute lymphoblastic leukemia of a B-cell lineage, or chronic lymphocytic leukemia of a B-cell lineage.

32. The combination therapy of Claim 24, wherein the CD40L antagonist is an anti-CD40L antibody or a fragment thereof.

33. The combination therapy of Claim 32, wherein the anti-CD40L antibody is IDEC-131 or a fragment thereof.

34. The combination therapy of Claim 32, wherein the anti-CD40L fragment is Fab, Fab', scFv or $F(ab')_2$.

35. The combination therapy of Claim 24, wherein the anti-CD20 antibody is RITUXAN® or a fragment thereof or B1 or a fragment thereof.

36. The combination therapy of Claim 28, wherein the chemotherapeutic agent for treating HD is any one or more of the following: an alkylating agent, a vinca alkaloid, procarbazine, methotrexate or prednisone.

37. The combination therapy of Claim 28, wherein the chemotherapeutic agent for treating NHL is any one or more of the following: an alkylating agent, cyclophosphamide, chlorambucil, 2-CDA, 2'-deoxycoformycin, fludarabine, cytosine arabinoside, cisplatin, etoposide or ifosfamide.

38. The combination therapy of Claim 28, wherein the combination of chemotherapeutic agents for treating HD is: MOPP, ABVD, ChlVPP, CABS, MOPP plus ABVD, MOPP plus ABV, BCVPP, VABCD, ABDIC, CBVD, PCVP, CEP, EVA, MOPLACE, MIME, MINE, CEM, MTX-CHOP, EVAP or EPOCH.

39. The combination therapy of Claim 28, wherein the combination of chemotherapeutic agents for treating NHL is: CVP, CHOP, C-MOPP, CAP-BOP, m-BACOD, ProMACE-MOPP, ProMACE-CytaBOM, MACOP-B, IMVP-16, MIME, DHAP, ESHAP, CEPP(B), or CAMP.

40. The combination therapy of Claim 28, wherein the chemotherapeutic agent for treating a B-cell leukemia is: anthracycline, cyclophosphamide, L-asparginase, a purine analog.

41. The combination therapy of Claim 28, wherein the combination of chemotherapeutic agents for treating a B-cell leukemia is: vincristine, prednisone, anthracycline and cyclophosphamide or asparginase; vincristine, prednisone, anthracycline, cyclophosphamide and asparginase; CHOP; CMP; CVP; COP or CAP.

42. A composition for the treatment of a $CD40^+$ malignancy comprising an (i) anti-CD40L antibody or antibody fragment thereof and at least one of the following: (ii) a radiolabeled antibody that binds CD40L, CD19, CD22, or CD20, (iii) an anti-CD20, an anti-CD19 antibody, an anti-CD22 antibody, or fragment thereof, or (iv) a chemotherapeutic agent or a chemotherapeutic combination.

43. The composition for the treatment of a $CD40^+$ malignancy of Claim 42 wherein the malignancy is a B-cell lymphoma or a B-cell leukemia.

44. The composition of Claim 43, wherein the B-cell leukemia is Hodgkin's Disease or NHL.

45. The composition of Claim 42, wherein the radiolabeled antibody is radiolabeled IDEC-131, RITUXAN®, or B1.

46. The composition of Claim 46, wherein the radiolabeled antibody is radiolabeled with ^{123}I, ^{125}I, ^{131}I, ^{111}In, ^{131}In, ^{32}P, ^{64}Cu, ^{67}Cu, ^{211}At, ^{177}Lu, ^{90}Y, ^{186}Re, ^{212}Pb, ^{212}Bi, ^{47}Sc, ^{105}Rh, ^{109}Pd, ^{153}Sm, ^{188}Re, ^{199}Au, ^{211}At, and ^{213}Bi.

47. The composition of Claim 44, wherein the NHL is low grade, intermediate grade or high grade.

48. The composition of Claim 44, wherein the NHL is selected from the NHL subtype group consisting of the following: small lymphocytic, follicular and predominantly small cleaved cell, follicular and mixed small cleaved and large cell type, follicular and predominantly large cell type, diffuse small cleaved cell, diffuse mixed small and large cell, diffuse large cell, large cell immunoblastic, lymphoblastic, small non-cleaved Burkitt's and non-Burkitt's type, AIDS-related lymphomas,

angioimmunoblastic lymphadenopathy, mantle cell lymphoma and monocytoid B-cell lymphoma.

49. The composition of Claim 42, wherein the anti-CD40L antibody is IDEC-131 or a fragment thereof.

50. The composition of Claim 42, wherein the anti-CD20 antibody is RITUXAN® or a fragment thereof or B1 or a fragment thereof.

51. The composition of Claim 43, wherein the chemotherapeutic agent for treating HD is any one or more of the following: an alkylating agent, a vinca alkaloid, procarbazine, methotrexate or prednisone.

52. The composition of Claim 44, wherein the chemotherapeutic agent for treating NHL is any one or more of the following: an alkylating agent, cyclophosphamide, chlorambucil, 2-CDA, 2'-deoxycoformycin, fludarabine, cytosine arabinoside, cisplatin, etoposide or ifosfamide.

53. The composition of Claim 44, wherein the combination of chemotherapeutic agents for treating HD is: MOPP, ABVD, ChlVPP, CABS, MOPP plus ABVD, MOPP plus ABV, BCVPP, VABCD, ABDIC, CBVD, PCVP, CEP, EVA, MOPLACE, MIME, MINE, CEM, MTX-CHOP, EVAP or EPOCH.

54. The composition of Claim 44, wherein the combination of chemotherapeutic agents for treating NHL is: CVP, CHOP, C-MOPP, CAP-BOP, m-BACOD, ProMACE-MOPP, ProMACE-CytaBOM, MACOP-B, IMVP-16, MIME, DHAP, ESHAP, CEPP(B), or CAMP.

55. The composition of Claim 43, wherein the chemotherapeutic agent for treating a B-cell leukemia is: anthracycline, cyclophosphamide, L-asparginase, a purine analog.

56. The composition of Claim 43, wherein the combination of chemotherapeutic agents for treating a B-cell leukemia is: vincristine, prednisone,

anthracycline and cyclophosphamide or asparginase; vincristine, prednisone, anthracycline, cyclophosphamide and asparginase; CHOP; CMP; CVP; COP or CAP.

57. A method of treating a B cell malignancy in a subject in need of such treatment comprising administering a therapeutically effective amount of at least one immunoregulating or immunomodulating antibody that is selected from the group consisting of an anti-CD23, anti-B7, anti-CD40, anti-CD40L and anti-CD4 antibody and at least B cell depleting antibody, and wherein said antibody administration is effected separately, in combination, and in either order of administration.

58. The method of Claim 57 wherein the B cell depleting antibody is selected from the group consisting of an anti-CD19, anti-CD20, anti-CD22 and anti-CD37 antibody.

59. The method of Claim 57 wherein B cell malignancy is non-Hodgkin's lymphoma.

60. The method of Claim 59 wherein said the NHL is selected from the subtype group consisting of: small lymphocytic, follicular and predominantly small cleaved cell, follicular and mixed small cleaved and large cell type, follicular and predominantly large cell type, diffuse small cleaved cell, diffuse mixed small and large cell, diffuse large cell, large cell immunoblastic, lymphoblastic, small non-cleaved Burkitt's and non-Burkitt's type, AIDS-related lymphomas, angioimmunoblastic lymphadenopathy, mantle cell lymphoma, and monocytoid B-cell lymphoma.

61. The method of Claim 60 wherein said NHL is high grade, low grade or intermediate grade.

62. The method of Claim 60 wherein said B cell depleting antibody is an anti-CD20 or anti-CD22 antibody.

63. The method of Claim 62 wherein said anti-CD20 antibody is RITUXAN®.

64. The method of Claim 62 wherein said anti-CD20 antibody is a human or humanized antibody.

65. The method of Claim 57 wherein the B cell malignancy is B cell lymphoma.

66. The method of Claim 1 wherein the B cell malignancy is a leukemia.

67. The method of Claim 66 wherein said leukemia is chronic lymphocytic leukemia, acute lymphoblastic leukemia or chronic B cell leukemia.

68. The method of Claim 57 wherein treatment comprises the administration of an anti-B7 antibody and an anti-CD20 antibody.

69. The method of Claim 68 wherein the anti-CD20 is RITUXAN®.

70. The method of Claim 68 wherein the anti-B7 antibody is a Primatized® antibody.

71. The method of Claim 70 wherein the anti-B7 antibody induces apoptosis of cancer cells.

72. The method of Claim 57 wherein the immunoregulatory antibody is administered after the B cell depleting antibody.

73. The method of Claim 57 wherein the immunoregulatory antibody is administered before the B cell depleting antibody.

74. The method of Claim 57 wherein the B cell depleting antibody and the immunoregulatory antibody are administered within about a month of each other.

75. The method of Claim 57 wherein the B cell depleting antibody and the immunoregulatory antibody are administered within about one week of each other.

76. The method of Claim 57 wherein the B cell depleting antibody and the imunoregulatory antibody are administered within about 1 day of each other.

77. The method of Claim 57 wherein is used to treat a B cell malignancy selected from the group consisting of relapsed Hodgkin's disease, resistant Hodgkin's disease high grade, low grade and intermediate grade non-Hodgkin's lymphomas, small lymphocytic/B cell chronic lymphocytic leukemia (SLL/B-CLL), lymhoplasmacytoid lymphoma (LPL), mantle cell lymphoma (MCL), follicular lymphoma (FL), diffuse large cell lymphoma (DLCL), Burkitt's lymphoma (BL), AIDS- related lymphomas, monocytic B cell lymphoma, angioimmunoblastic lymphoadenopathy, small lymphocytic; follicular, diffuse large cell; diffuse small cleaved cell; large cell immunoblastic lymphoblastoma; small, non-cleaved; Burkitt's and non-Burkitt's; follicular, predominantly large cell; follicular, predominantly small cleaved cell; and follicular, mixed small cleaved and large cell lymphomas.

78. The method of Claim 77 wherein said B cell malignancy is Hodgkin's disease.

79. The method of Claim 57 wherein either or both antibody is attached to a radiolobel.

80. The method of Claim 57 which further comprises chemotherapy or radiation therapy.

81. The method of Claim 57 which includes administration of a non-antibody antagonist specific to CD40L or B7.

82. A method of treating non-Hodgkin's lymphoma comprising administering separately or in combination a therapeutically effective amount of an antibody to B7 and a B cell depleting anti-CD20 or anti-CD22 antibody.

83. The method of Claim 82 wherein said anti-CD20 antibody is RITUXAN®.

84. The method of Claim 82 wherein said anti-B7 antibody does not inhibit the interaction of B7 antigen with CTLA4.

85. The method of Claim 84 wherein said antibody to B7 is a human, humanized, primatized or primate antibody.

86. The method of Claim 82 wherein said NHL is high grade, low grade or intermediate grade.

87. The method of Claim 82 which includes administration of a radiolabeled antibody.

88. A method of treating leukemia comprising administering a therapeutically effective amount of an anti-B7 antibody and a B cell depleting antibody specific to CD20 or CD22.

89. The method of Claim 88 wherein said anti-CD20 antibody is RITUXAN® (antibody provided by ATCC 69119).

90. The method of Claim 88 wherein said leukemia is chronic lymphocytic leukemia, acute lymphoblastic leukemia or chronic B cell leukemia.

91. The method of Claim 88 wherein either or both of said antibodies are chimeric, bispecific, human or humanized antibodies.

92. The method of Claim 57 wherein the anti-B7 antibody is a depleting antibody.

93. The method of Claim 57 wherein the anti-B7 antibody is a non-depleting antibody.

94. The method of Claim 57 wherein the anti-B7 antibody specifically binds B7.1 (CD80).

95. The method of Claim 57 wherein the anti-B7 antibody specifically binds B7.2 (CD86).

96. The method of Claim 57 which includes administration of a radiolabeled anti-CD22 or anti-CD22 antibody.

97. The method of Claim 96 wherein said radiolabel is yttrium.

98. The method of Claim 97 wherein said radiolabeled anti-CD20 is yttrium-labeled RITUXAN® or yttrium-labeled 2B8.

99. The method of Claim 82 wherein the anti-B7 antibody is a non-depleting antibody.

100. The method of Claim 82 wherein the anti-B7 antibody is a depleting antibody.

101. The method of Claim 82 wherein the non-Hodgkin's lymphoma is selected from small lymphocytic, follicular and predominantly small cleaved cell, follicular and mixed small cleaved and large cell type, follicular and predominantly large cell type, diffuse small cleaved cell, diffuse mixed small and large cell, diffuse large cell, large cell immunoblastic, lymphoblastic, small non-cleaved Burkitt's and non-Burkitt's type, AIDS-related lymphomas, angioimmunoblastic lymphadenopathy, mantle cell lymphoma, and monocytoid B-cell lymphoma.

102. The method of Claim 57 which includes chemotherapy.

103. The method of Claim 82 which includes chemotherapy.